

Atty. Docket No.: PG3119US2

REMARKS

Claims 1-10 are pending in this application. New claims 11-23 are added to more completely defined the invention. New claims 11-23 are dependent on claim 1 and thus raise no new issues of patentability. Claim 1 has been amended to correct a typographic error in the claim. Accordingly, Claims 1-23 are before the Examiner for examination.

Obviousness-Type Double Patenting Rejection

Claims 1-10 are rejected under the judicially created doctrine of obviousness type double patenting over Claims 30 to 32 of U.S. Patent 6,391,874. Included herewith is a terminal disclaimer in compliance with 37 C.F.R. 1.321(c), which disclaims the terminal portion of the term of the present invention to the expiration date of U.S. Patent 6,391,874.

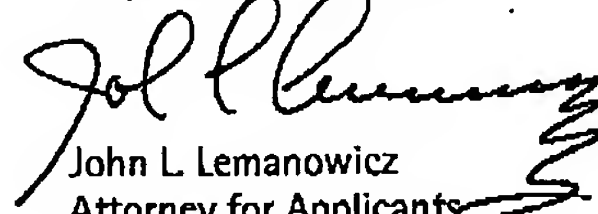
Applicants assert that the rejection is overcome by the filing of the terminal disclaimer and respectfully request it be withdrawn.

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CONCLUSION

The points and concerns of the Examiner having been addressed in full, Applicants respectfully submit that the instant application is in condition for allowance, which action is respectfully requested. Should any issues remain unresolved in this application which would bar issuance, the Examiner is invited to contact the undersigned Attorney at (919) 483-8247, to discuss such issues. Applicants believe that no fees are due in connection with the filing of this paper other than those specifically authorized herewith. However, should any other fees be deemed necessary to effect the timely filing of this paper the Commissioner is hereby authorized to charge such fees to Deposit Account No. 07-1392.

Respectfully submitted,



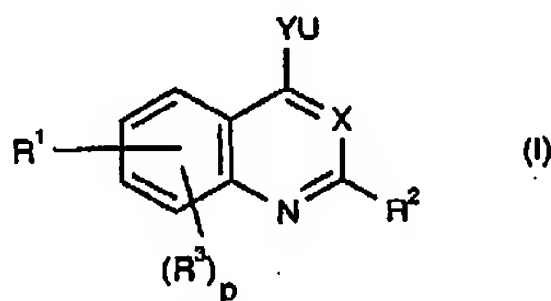
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Amended Claims - Marked Up Version

1. (Currently Amended) A method of treating a susceptible cancer in a human or animal subject [mammal], comprising administering to said subject an effective amount of a compound of formula (I):



or a salt or solvate thereof;

wherein X is N or CH;

Y is a group $W(\text{CH}_2)$, $(\text{CH}_2)W$, or W , in which W is O, $\text{S}(\text{O})_m$ wherein m is 0, 1 or 2, or NR^a wherein R^a is hydrogen or a C_{1-8} alkyl group;

R^1 represents a 5- or 6-membered heterocyclic ring containing 1 to 4 heteroatoms selected from N, O or $\text{S}(\text{O})_m$, wherein m is as defined above, with the provisos that the ring does not have two adjacent O or $\text{S}(\text{O})_m$ atoms and that where the ring has only N as heteroatom(s) the ring is C-linked to the quinazoline or quinoline ring, R^1 being optionally substituted by one or more R^3 groups;

each R^3 is independently selected from the group consisting of amino, hydrogen, halogen, hydroxy, nitro, carboxy, formyl, cyano, trifluoromethyl, trifluoromethoxy, carbamoyl, ureldo, guanidino, C_{1-8} alkyl, C_{1-8} alkoxy, C_{3-8} cycloalkoxy, C_{4-8} alkylcycloalkoxy, C_{1-8} alkylcarbonyl, C_{1-8} alkoxycarbonyl, N-C_{1-4} alkylcarbamoyl, N,N-di-[C_{1-4} alkyl]carbamoyl, hydroxyamino, C_{1-4} alkoxyamino, C_{2-4} alkanoyloxyamino, C_{1-4}

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alkylamino, di-[C₁₋₄ alkyl]amino, di-[C₁₋₄ alkyl]amino-C₁₋₄ alkylene-(C₁₋₄ alkyl)amino, C₁₋₄ alkylamino-C₁₋₄ alkylene-(C₁₋₄ alkyl)amino, hydroxy-C₁₋₄ alkylene-(C₁₋₄ alkyl)amino, phenyl, phenoxy, 4-pyridon-1-yl, pyrrolidin-1-yl, imidazol-1-yl, piperidino, morpholino, thiomorpholino, thiomorpholino-1-oxide, thiomorpholino-1,1-dioxide, piperazin-1-yl, 4-C₁₋₄ alkylpiperazin-1-yl, dioxolanyl, C₁₋₈ alkylthio, arylthio, C₁₋₄ alkylsulphinyl, C₁₋₄ alkylsulphonyl, arylsulphonyl, arylsulphinyl, halogeno-C₁₋₄ alkyl, hydroxy-C₁₋₄ alkyl, C₂₋₄ alkanoyloxy-C₁₋₄ alkyl, C₁₋₄ alkoxy-C₁₋₄ alkyl, carboxy-C₁₋₄ alkyl, formyl-C₁₋₄ alkyl, C₁₋₄ alkoxycarbonyl-C₁₋₄-alkyl, carbamoyl-C₁₋₄ alkyl, N-C₁₋₄ alkylcarbamoyl-C₁₋₄alkyl, N,N-di-[C₁₋₄ alkyl]carbamoyl-C₁₋₄alkyl, amino-C₁₋₄ alkyl, C₁₋₄ alkylamino-C₁₋₄ alkyl, di-[C₁₋₄ alkyl]amino-C₁₋₄ alkyl, phenyl-C₁₋₄ alkyl, 4-pyridon-1-yl-C₁₋₄ alkyl, pyrrolidin-1-yl-C₁₋₄ alkyl, imidazol-1-yl-C₁₋₄ alkyl, piperidino-C₁₋₄ alkyl, morpholino-C₁₋₄ alkyl, thiomorpholino-C₁₋₄ alkyl, thiomorpholino-1-oxide-C₁₋₄alkyl, thiomorpholino-1,1-dioxide-C₁₋₄alkyl, piperazin-1-yl-C₁₋₄alkyl, 4-C₁₋₄ alkylpiperazin-1-yl-C₁₋₄ alkyl, hydroxy-C₂₋₄ alkoxy-C₁₋₄ alkyl, C₁₋₄ alkoxy-C₂₋₄ alkoxy-C₁₋₄ alkyl, hydroxy-C₂₋₄ alkylamino-C₁₋₄ alkyl, C₁₋₄ alkoxy-C₂₋₄ alkylamino-C₁₋₄ alkyl, C₁₋₄ alkylthio-C₁₋₄ alkyl, C₁₋₄ alkylsulphinyl-C₁₋₄ alkyl, C₁₋₄ alkylsulphonyl-C₁₋₄ alkyl, hydroxy-C₂₋₄ alkylthio-C₁₋₄ alkyl, C₁₋₄ alkoxy-C₂₋₄ alkylthio-C₁₋₄ alkyl, phenoxy-C₁₋₄ alkyl, anilino-C₁₋₄ alkyl, phenylthio-C₁₋₄ alkyl, cyano-C₁₋₄ alkyl, halogeno-C₂₋₄ alkoxy, hydroxy-C₂₋₄ alkoxy, C₂₋₄ alkanoyloxy-C₂₋₄ alkoxy, C₁₋₄ alkoxy-C₂₋₄ alkoxy, carboxy-C₁₋₄ alkoxy, formyl-C₁₋₄ alkoxy, C₁₋₄ alkoxycarbonyl-C₁₋₄ alkoxy, carbamoyl-C₁₋₄ alkoxy, N-C₁₋₄ alkylcarbamoyl-C₁₋₄ alkoxy, N,N-di-[C₁₋₄ alkyl]carbamoyl-C₁₋₄ alkoxy, amino-C₂₋₄ alkoxy, C₁₋₄ alkylamino-C₂₋₄ alkoxy, di-[C₁₋₄ alkyl]amino-C₂₋₄ alkoxy, di-[C₁₋₄ alkyl-C₂₋₄ alkoxy]amino-C₂₋₄ alkoxy, C₂₋₄ alkanoyloxy, hydroxy-C₂₋₄ alkanoyloxy, C₁₋₄alkoxy-C₂₋₄ alkanoyloxy, phenyl-C₁₋₄ alkoxy, phenoxy-C₂₋₄ alkoxy, anilino-C₂₋₄ alkoxy, phenylthio-C₂₋₄ alkoxy, 4-pyridon-1-yl-C₂₋₄ alkoxy, piperidino-C₂₋₄ alkoxy, morpholino-C₂₋₄ alkoxy, thiomorpholino-C₂₋₄

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alkoxy, thiomorpholino-1-oxide-C₂₋₄ alkoxy, thiomorpholino-1,1-dioxide-C₂₋₄ alkoxy, piperazin-1-yl-C₂₋₄ alkoxy, 4-C₁₋₄ alkylpiperazin-1-yl-C₂₋₄ alkoxy, pyrrolidin-1-yl-C₂₋₄ alkoxy, imidazol-1-yl-C₂₋₄ alkoxy, halogeno-C₂₋₄ alkylamino, hydroxy-C₂₋₄ alkylamino, C₂₋₄ alkanoyloxy-C₂₋₄ alkylamino, C₁₋₄ alkoxy-C₂₋₄ alkylamino, carboxy-C₁₋₄ alkylamino, C₁₋₄ alkoxycarbonyl-C₁₋₄ alkylamino, carbamoyl-C₁₋₄ alkylamino, N-C₁₋₄ alkylcarbamoyl-C₁₋₄ alkylamino, N,N-di-[C₁₋₄ alkyl]carbamoyl-C₁₋₄ alkylamino, amino-C₂₋₄ alkylamino, C₁₋₄ alkylamino-C₂₋₄ alkylamino, di-[C₁₋₄alkyl]amino-C₂₋₄ alkylamino, phenyl-C₁₋₄ alkylamino, phenoxy-C₂₋₄ alkylamino, anilino-C₂₋₄ alkylamino, 4-pyridon-1-yl- C₂₋₄ alkylamino, pyrrolidin-1-yl-C₂₋₄ alkylamino, imidazol-1-yl-C₂₋₄ alkylamino, piperidino-C₂₋₄ alkylamino, morpholino-C₂₋₄ alkylamino, thiomorpholino-C₂₋₄ alkylamino, thiomorpholino-1-oxide-C₂₋₄ alkylamino, thiomorpholino-1,1-dioxide-C₂₋₄ alkylamino, piperazin-1-yl-C₂₋₄alkylamino, 4-(C₁₋₄alkyl)piperazin-1-yl-C₂₋₄alkylamino, phenylthio-C₂₋₄ alkylamino, C₂₋₄ alkanoylamino, C₁₋₄ alkoxycarbonylamino, C₁₋₄ alkylsulphonylamino, C₁₋₄ alkylsulphinylamino, benzamido, benzenesulphonamido, 3-phenylureido, 2-oxopyrrolidin-1-yl, 2,5-dioxopyrrolidin-1-yl, halogeno-C₂₋₄ alkanoylamino, hydroxy-C₂₋₄ alkanoylamino, hydroxy-C₂₋₄ alkanoyl-(C₁₋₄ alkyl)-amino, C₁₋₄ alkoxy-C₂₋₄ alkanoylamino, carboxy-C₂₋₄ alkanoylamino, C₁₋₄ alkoxycarbonyl-C₂₋₄ alkanoylamino, carbamoyl-C₂₋₄ alkanoylamino, N-C₁₋₄ alkylcarbamoyl-C₂₋₄ alkanoylamino, N,N-di-[C₁₋₄ alkyl]carbamoyl-C₂₋₄ alkanoylamino, amino-C₂₋₄ alkanoylamino, C₁₋₄ alkylamino-C₂₋₄ alkanoylamino or di-[C₁₋₄ alkyl]amino-C₂₋₄ alkanoylamino; and wherein said benzamido or benzenesulphonamido substituent or any anilino, phenoxy or phenyl group on a R³ substituent may optionally have one or two halogeno, C₁₋₄ alkyl or C₁₋₄ alkoxy substituents; and wherein any substituent having a heterocyclic ring may optionally have one or two halogeno, C₁₋₄ alkyl or C₁₋₄ alkoxy substituents on said ring; and wherein any substituent having a heterocyclic ring may optionally have one or two oxo or thioxo substituents on said ring;

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or R^3 represents a group selected from $M^1-M^2-M^3-M^4$, M^1-M^5 or $M^1-M^2-M^3-M^6$

wherein

M^1 represents a C_{1-4} alkyl group, wherein optionally a CH_2 group is replaced by a CO group;

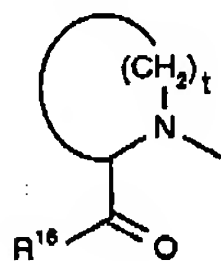
M^2 represents NR^{12} or $CR^{12}R^{13}$, in which R^{12} and R^{13} each independently represent H or C_{1-4} alkyl;

M^3 represents a C_{1-4} alkyl group;

M^3 represents a C_{1-4} alkyl group or is absent;

M^4 represents CN , $NR^{12}S(O)_mR^{13}$, $S(O)_mNR^{14}R^{15}$, $CONR^{14}R^{15}$, $S(O)_mR^{13}$ or CO_2R^{13} , in which R^{12} , R^{13} and m are as defined above and R^{14} and R^{15} each independently represent H or C_{1-4} alkyl, or R^{14} and R^{15} together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally containing 1 or 2 additional heteroatoms selected from N, O or $S(O)_m$ in which ring any nitrogen atom present may optionally be substituted with a C_{1-4} alkyl group, and which ring may optionally have one or two oxo or thioxo substituents;

M^5 represents the group $NR^{14}R^{15}$, wherein R^{14} and R^{15} are as defined above, or M^5 represents the group



in which t represents 2 to 4 and R^{16} represents OH, OC_{1-4} alkyl or $NR^{14}R^{15}$;

and

M^6 represents a C_{3-6} cycloalkyl group, the group $NR^{14}R^{15}$, wherein R^{14} and R^{15} are as defined above, or a 5- or 6-membered heterocyclic ring system containing 1 to 4 heteroatoms selected from N, O or S;

and p is 0 to 3; or when p is 2 or 3, two adjacent R^3 groups together form an optionally substituted methylenedioxy or ethylenedioxy group;

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R² is selected from the group consisting of hydrogen, halogen, trifluoromethyl, C₁₋₄ alkyl and C₁₋₄ alkoxy;

U represents phenyl or a 5 to 10-membered mono or bicyclic ring system in which one or more of the carbon atoms is optionally replaced by a heteroatom independently selected from N, O and S(O)_m, wherein m is 0, 1 or 2, and wherein U is substituted by at least one independently selected R⁶ group and U is optionally substituted by at least one independently selected R⁴ group;

each R⁴ is independently hydrogen, hydroxy, halogen, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino, di-[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulphinyl, C₁₋₄ alkylsulphonyl, C₁₋₄ alkylcarbonyl, C₁₋₄ alkylcarbamoyl, di-[C₁₋₄ alkyl] carbamoyl, carbamyl, C₁₋₄ alkoxycarbonyl, cyano, nitro or trifluoromethyl;

each R⁶ is independently a group ZR⁷ wherein Z is joined to R⁷ through a (CH₂)_p group in which p is 0, 1 or 2 and Z represents a group V(CH₂), V(CF₂), (CH₂)V, (CF₂)V, V(CRR'), V(CHR) or V where R and R' are each C₁₋₄ alkyl and in which V is a hydrocarbyl group containing 0, 1 or 2 carbon atoms, carbonyl, dicarbonyl, CH(OH), CH(CN), sulphonamide, amide, O, S(O)_m or NR^b where R^b is hydrogen or R^b is C₁₋₄ alkyl; and R⁷ is an optionally substituted C₃₋₆ cycloalkyl; or an optionally substituted 5, 6, 7, 8, 9 or 10-membered carbocyclic or heterocyclic moiety;

or R⁶ is a group ZR⁷ in which Z is NR^b, and NR^b and R⁷ together form an optionally substituted 5, 6, 7, 8, 9 or 10-membered carbocyclic or heterocyclic moiety.